PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 15 August 2000 (15.08.00)	
International application No. PCT/US99/30066	**Applicant's or agent's file reference** CHAIN4APCT
International filing date (day/month/year) 17 December 1999 (17.12.99)	**Priority date** (day/month/year) 17 December 1998 (17.12.98)
Applicant CHAIN, Daniel, G. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

13 July 2000 (13.07.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Juan Cruz
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
CHAIN4APCT		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 99/ 30066	17/12/1999	17/12/1998
Applicant		
MINDSET BIOPHARMACEUTICALS USA INC et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [ ] the text is approved as submitted by the applicant.

   [X] the text has been established by this Authority to read as follows:

   IMPROVING MENTAL PERFORMANCE PERFORMANCE BY INCREASING BRAIN INSULIN SENSITIVITY

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawing** to be published with the abstract is Figure No. _____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-5, 10,11,15-17 and 19-22 relate to compounds defined by reference to desirable characteristics or properties, e.g. "...an agent to improve insulin sensitivity in the brain." (claim 1), "...the agent activates the PPAR gamma receptor." (claim 10), an agent which "...activates a RxR receptor that forms a heterodimer with a PPAR gamma receptor."(claim 16), "...the agent interacts with the insulin transduction process" (claim 20), "an agent to improve mental performance" (claim 21) and "cerebral enhancers" (claim 22). The claims cover all compounds having these characteristics or properties, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Additionally, PPAR and RxR receptors are not adequately defined in the application so it is not possible to deduce which compounds are meant to be included in the definition "activators" of RxR, PPAR gamma or PPAR alpha receptors.

Moreover, expressions such as "a thiazolidinedione", "an oxyzolidinedione", "a substituted 4-hydroxy -phenylalcanoic acid derivative", "a natural product or is derived from a natural product", "a prodrug" etc. relate to a rather elevated number of possible compounds. Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Furthermore present claims 1-22 and 23-30 relate to a use defined as "...for improving mental performance in patients having symptoms of reduced mental performance and are (sic) neither in a state of non-insulin dependent diabetes nor a state of general impaired glucose tolerance". The use of these parameters in the present context is considered to lead to a lack of clarity within the meaning of Article 6 PCT. It is impossible to compare the parameters the applicant has chosen to employ with what is set out in the prior art. The lack of clarity is such as to render a meaningful complete search impossible. Consequently, the search has been restricted to the use of the claimed compounds.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds specifically mentioned in the claims and their use related to improving mental performance with due regard to the general idea underlying the application.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/30066

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/425 A61K31/44 A61K31/42

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	COMBS, C.K. ET AL: "Inflammatory mechanisms in Alzheimer's disease: Inhibition of beta.amyloid -stimulated proinflammatory responses and neurotoxicity by PPAR.gamma agonists" THE JOURNAL OF NEUROSCIENCE, vol. 20, no. 2, 15 January 2000 (2000-01-15), pages 558-567, XP000933946 the whole document	1-30
E	WO 00 32190 A (CASE WESTERN RESERVE UNIVERSITY) 8 June 2000 (2000-06-08) the whole document	1-13,15, 18,20,23

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
15 August 2000	23/08/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Mair, J

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
E	WO 00 23451 A (NOVO NORDISK A/S) 27 April 2000 (2000-04-27) the whole document especially page 1, line 23 ---	1-5,10, 11,13, 15,19, 20,23
E	WO 00 23445 A (NOVO NORDISK A/S) 27 April 2000 (2000-04-27) the whole document especially page 1, line 23 ---	1-5,10, 11,13, 15,19, 20,23
E	WO 00 23417 A (NOVO NORDISK A/S) 27 April 2000 (2000-04-27) the whole document especially page 1, line 23 ---	1-5,10, 11,13, 15,19, 20,23
E	WO 00 23416 A (NOVO NORDISK A/S) 27 April 2000 (2000-04-27) the whole document especially page 1, line 23 ---	1-5,10, 11,13, 15,19, 20,23
E	WO 00 23415 A (NOVO NORDISK A/S) 27 April 2000 (2000-04-27) the whole document especially page 1, line 24 ---	1-5,10, 11,13, 15,19, 20,23
E	WO 00 23407 A (GLAXO GROUP LIMITED) 27 April 2000 (2000-04-27) the whole document ---	1-5,10, 11,13, 15-17, 19,20,23
E	US 6 028 088 A (PERSHADSINGH ET AL) 22 February 2000 (2000-02-22) the whole document especially column 33, Table V and VI; claims 30 and 31 --- -/--	1-6,10, 11, 15-17, 19-23

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
P,X	KITAMURA, Y. ET AL: "Increased expression of cyclooxygenases and peroxisome proliferator-activated receptor.gamma in Alzheimer's disease brains" BIOCHEMICAL AND BIOPHYSICAL RESERACH COMMUNICATIONS, vol. 254, no. 3, 27 January 1999 (1999-01-27), pages 582-586, XP000929650 cited in the application the whole document	1-5,10, 11,13, 15,16, 19,23
P,X	WO 99 16758 A (DR. REDDY'S RESEARCH FOUNDATION) 8 April 1999 (1999-04-08) the whole document especially page 96, claim 22, line 25	1-5,10, 11,13, 15,19,20
P,X	WO 99 38850 A (DR. REDDY'S RESEARCH FOUNDATION) 5 August 1999 (1999-08-05) the whole document especially page 106, claim 21, line 9-10	1-5,10, 11,13, 15,19,20
P,X	WO 99 20614 A (DR. REDDY'S RESEARCH FOUNDATION) 29 April 1999 (1999-04-29) the whole document especially page 113, claim 23, line 9-10	1-5,10, 11,13, 15,19,20
X	US 5 556 843 A (ROMEO ET AL) 17 September 1996 (1996-09-17) cited in the application the whole document especially column 2, line 4-7; column 4, claims 6 and 7	1-5,23
A	WO 97 31907 A (GLAXO GROUP LTD.) September 1997 (1997-09) cited in the application the whole document	11,12
A	US 5 039 794 A (WIER ET AL) 13 August 1991 (1991-08-13) cited in the application the whole document	28
A	US 4 540 564 A (BODOR) 10 September 1985 (1985-09-10) cited in the application the whole document	26,27

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	DUELLI, R. ET AL: "Intracerebroventricular injection of streptozotocin induces discrete local changes in cerebral glucose utilization in rats" INTERNATIONAL JOURNAL OF DEVELOPMENTAL NEUROSCIENCE, vol. 12, no. 8, 1994, pages 737-747, XP000933903 cited in the application the whole document	1-30
A	MUKHERJEE, R. ET AL: "Sensitization of diabetic and obese mice to insulin by retinoid X receptor agonists" NATURE, vol. 386, 1997, pages 407-410, XP002081440 cited in the application the whole document	5,15-17
A	BLUM-DEGEN D. ET AL: "Altered regulation of brain glucose metabolism as a cause of neurodegenerative disorders?" JOURNAL OF NEURAL TRANSMISSION, vol. suppl. 46, 1995, pages 139-147, XP000933904 cited in the application the whole document	1-30
A	GRANNEMAN, J. ET AL: "Member of the Peroxisome Proliferator-Activated Receptor family of transcription factors is differentially expressed by oligodendrocytes" JOURNAL OF NEUROSCIENCE RESEARCH, vol. 51, 1998, pages 563-573, XP000933914 cited in the application the whole document especially page 564, lefthand column, line 18-24	1-30
A	HOYER, S. ET AL: "Brain glucose metabolism is controlled by amplification and desensitization of the neuronal insulin receptor" ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, vol. 777, 1996, pages 374-379, XP000933907 cited in the application the whole document	1-30

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
US 99/30066

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 0032190	A	08-06-2000	NONE		
WO 0023451	A	27-04-2000	AU	6325799 A	08-05-2000
WO 0023445	A	27-04-2000	AU	6325599 A	08-05-2000
WO 0023417	A	27-04-2000	AU	6325899 A	08-05-2000
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
US 99/30066

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		ZA 8303521 A	24-12-1984
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